DIPHENHYDRAMINE HCl

SONIPHEN™

50 mg CAPSULE & 50 mg/mL SOLUTION FOR INJECTION

ANTIHISTAMINE / ANTICHOLINERGIC

FORMULATIONS

Each capsule contains:
Diphenhydramine HCl, USP ……..50 mg

Each mL solution for injection contains:
Diphenhydramine HCl, USP ……..50 mg

DESCRIPTION OF THE PRODUCTS

Diphenhydramine HCl (Soniphen) 50 mg is a hard gelatin capsule with scarlet opaque capsule cap and body.
Diphenhydramine HCl (Soniphen) injection is a clear, colorless, sterile aqueous solution, free from extraneous matter.

PHARMACOLOGY

Diphenhydramine HCl is an ethanolamine antihistamine with anticholinergic (antimuscarinic), antitussive, anti-emetic, anti-vertigo, sedative and hypnotic properties. Diphenhydramine acts predominantly as a competitive but reversible inhibitor of histamine at the H_1 receptor sites. The antitussive effect of diphenhydramine is due to a central mechanism involving suppression of the medullary cough center.The antiemetic and anti-motion sickness effects of diphenhydramine result from its central anticholinergic and central nervous system (CNS) depressant properties. Likewise, its activity on parkinsonian syndrome and drug-induced extrapyramidal reactions are related to its central anticholinergic effects.Anti-vertigo action is by central antimuscarinic effect on the vestibular apparatus and the integrative vomiting center and medullary chemoreceptor trigger zone of the mid brain.The exact mechanism for CNS depressant action is not known, but it is thought to cause indirect reduction of stimuli to the brain stem reticular formation.

PHARMACOKINETICS

Injectable diphenhydramine has a rapid onset of action. After intravenous (IV) injection of a single 50 mg dose over a 1-minute period in healthy adults, plasma diphenhydramine concentration one hour after the injection ranged from 99-196 ng/mL. A single oral dose of diphenhydramine HCl is quickly absorbed with maximum activity occurring in approximately one hour. The duration of activity after an average dose of diphenhydramine is from 4-6 hours. After single oral doses of 50 and 100 mg in healthy adults, peak plasma concentrations of 37-83 ng/mL and 81-159 ng/mL, respectively, have been reported. After oral administration of diphenhydramine dosages of 25 mg every 4 hours or 50 mg every 6 hours, peak steady-state plasma concentrations of the drug were 55 or 85 ng/mL, respectively, and minimum steady-state plasma concentrations were 27.5 or 30 ng/mL, respectively. Diphenhydramine is widely distributed throughout the body, including the CNS. The drug crosses the placenta and has been detected in milk, although the extent of distribution into milk has not been quantified. Diphenhydramine is approximately 80-85% bound to plasma proteins *in vitro.* Less extensive protein binding of the drug has been reported in healthy Asian adults and in adults with liver cirrhosis. After IV administration, diphenhydramine's volume of distribution is 4.5 L/kg, its half-life 8.4 hours, and its clearance, 6.2 mL/min/kg. In a study among Caucasian and Asian patients, diphenhydramine 50 mg given orally showed greater peak plasma concentrations among Asians compared with Caucasians. Plasma protein binding was 85.2% in Caucasians and 76% in Asians. Asians had higher mean volumes of distribution and mean clearance values.Diphenhydramine is rapidly and almost completely metabolized. After oral administration, the drug undergoes substantial first-pass metabolism in the liver. Diphenhydramine appears to be metabolized principally to diphenylmethoxyacetic acid, which may further undergo conjugation. The drug also undergoes dealkylation to form the N-demethyl and N, N-didemethyl derivatives. Diphenhydramine and its metabolites are excreted principally in urine. Plasma concentrations of diphenhydramine appear to decline in a monophasic manner, although some pharmacokinetic data suggest a polyphasic elimination. The terminal elimination half-life of diphenhydramine has not been fully explained, but appears to range from 2.4-9.3 hours in healthy adults.

INDICATIONS

Antihistamine:

- For the relief of symptoms associated with seasonal, perennial, vasomotor rhinitis
- For mild, uncomplicated allergic skin manifestations of urticaria and angioedema
- Dermatographism
- For allergic conjunctivitis due to foods
- For amelioration of allergic reactions to blood or plasma
- As therapy for anaphylactic reactions adjunctive to epinephrine and other standard measures after acute manifestations have been controlled.

Antiparkinsonism:

For parkinsonism (including drug-induced) in the elderly unable to tolerate more potent agents; mild cases of parkinsonism (including drug-induced) in other age groups; in other cases of parkinsonism (including drug-induced) in combination with centrally acting anticholinergic agents.

Nighttime Sleep-Aid:

For the short-term management of insomnia

Antitussive:

For the relief of cough caused by minor throat and bronchial irritation such as may occur with the common colds, inhaled irritants or allergy.

Antiemetic/Motion Sickness:

For the prevention and treatment of nausea, vomiting, and/or dizziness associated with motion sickness.

DOSAGE AND ADMINISTRATION

Recommended Adult Oral Diphenhydramine Dose

Indications	Adult Oral Dose
	To be taken preferably with meals or with milk.
Antihistamine	1 capsule every 6 hours. Maximum: 300 mg in 24 hours.
Antiparkinsonism	1 capsule every 6 hours.
Nighttime Sleep Aid	1 capsule 20 minutes before going to bed.
Antitussive	1 capsule every 8 hours. Maximum: 300 mg in 24 hours.
Motion Sickness	1 capsule given 30 minutes before exposure to motion. Subsequent doses may be given every 6 hours before meals and at bedtime for the duration of the exposure. Maximum: 300 mg in 24 hours
	Or, as prescribed by a physician.

For intravenous (IV) or deep intramuscular (IM) administration only:

General Dosing Recommendations:

- Inspect visually for particulate matter and discoloration prior to administration, whenever solution and container permit.
- Individualize dosage according to the needs and response of the patient.
- Strict aseptic technique should be observed when drawing up the contents of the ampule. If injection ampules become contaminated, they have the potential to become a source of infection to patients.

Recommended Diphenhydramine IV or IM Dose	
CHILDREN	**ADULTS**
Usual Dose: 5 mg/kg body weight/day or 150 mg/m^2/day Divide daily dose into four doses given every 6 hours, administered IV at a rate generally not exceeding 25 mg/minute, or deep IM **Maximum Dose:** 300 mg in 24 hours	**Usual Dose:** 10 to 50 mg per dose, IV or deep IM; in a few patients up to 100 mg may be required. Rate of IV administration should not exceed 25 mg/minute. **Maximum Dose:** 400 mg in 24 hours
Or, as prescribed by a physician.	

Dosing in Patients with Renal Failure: In patients with renal failure, dosage intervals should be increased from 6 hours to 12 hours depending on the degree of renal impairment.

CONTRAINDICATIONS

- Hypersensitivity to diphenhydramine or any ingredient in the product
- Narrow angle glaucoma
- Stenosing peptic ulcer and pyloroduodenal obstructions predispose the patient to an increased risk of gastrointestinal (GI) obstruction. Agents with anticholinergic properties such as diphenhydramine reduce the tone and motility of the GI tract and thus increase the risk of worsening/contributing to GI obstruction.
- Diphenhydramine injection should not be used as a local anesthetic because of the risk of local necrosis
- Asthma attack
- Prostatic hypertrophy
- Bladder-neck obstruction
- Porphyria
- Do not use in premature infants and neonates
- Do not use in breastfeeding women

WARNINGS AND PRECAUTIONS

- Diphenhydramine can cause marked drowsiness; it severely impairs driving performance in standard off the road tests. Patients should avoid driving or performing other tasks requiring complete mental alertness.
- Diphenhydramine should not be taken with other antihistamines, sedatives or tranquilizers except on medical advice.
- Patients should be advised to avoid alcoholic beverages while taking this product. Alcohol potentiates the sedative effects of diphenhydramine.
- Patients should be advised to avoid using diphenhydramine for self-medication for longer than 7-10 nights and to consult a physician if insomnia persists continuously for longer than two weeks because insomnia may be indicative of a serious underlying physical, emotional, or psychological condition requiring medical attention.
- Do not use with any other product containing diphenhydramine, including topical formulations.
- Caution should be exercised if given to patients with liver disease (the terminal half-life of diphenhydramine may be prolonged in cirrhotic patients), glaucoma, urinary retention, myasthenia gravis, seizure disorders, hyperthyroidism, cardiovascular disease, or hypertension.
- Local necrosis has been associated with subcutaneous or intradermal use of IV diphenhydramine.

DRUG INTERACTIONS

- **Alcohol and other CNS depressants including barbiturates, tranquilizers, hypnotics, sedatives, antianxiety agents, and narcotic analgesics -** have additive effects with antihistamines. Dosage adjustments of CNS depressants may be necessary to avoid profound CNS depression.
- **Monoamine oxidase inhibitors (MAOI) (phenelzine, tranylcypromine, isocarboxazid, furazolidone, procarbazine) -** may prolong and intensify the anticholinergic and CNS depressant effects of diphenhydramine. Diphenhydramine should be used with caution with MAOIs or within two weeks of stopping a MAOI.
- **Anticholinergic drugs (e.g., atropine) -** may potentiate diphenhydramine's anticholinergic side effects.
- **ß-blockers (metoprolol, carvedilol, labetalol, propranolol, timolol) -** Diphenhydramine increases the plasma concentrations and cardiovascular effects of these drugs.
- **PAS (4-aminosalicylic acid) -** Diphenhydramine administration significantly reduces absorption of the antituberculosis agent PAS from the GI tract.

STATEMENT ON USAGE FOR HIGH RISK GROUPS

- **PREGNANCY AND LACTATION**

  Pregnancy: ***Pregnancy Category B.*** Diphenhydramine crosses the placental barrier and has been reported to cause jaundice and extrapyramidal symptoms in infants whose mothers received the drug during pregnancy. Drug therapy should be discontinued one to two weeks before the delivery to avoid these effects in the neonate. Therefore, diphenhydramine should be used in pregnancy only if the potential benefit justifies the potential risk to the fetus.

  Lactation : Diphenhydramine is excreted in human milk. Therefore, use of diphenhydramine when breastfeeding is not recommended.
- **PEDIATRICS**

  As in adults, antihistamines may diminish mental alertness in children. In the young child, particularly, they may produce excitation.
- **GERIATRICS**

  Antihistamines are more likely to cause dizziness, sedation, and hypotension in elderly patients.

ADVERSE EFFECTS/UNDESIRABLE EFFECTS

General: Urticaria, drug rash, anaphylactic shock, photosensitivity, excessive perspiration, chills, dryness of mouth, nose and throat
Cardiovascular: Hypotension, headache, palpitations, tachycardia, extrasystoles
Hematologic: Hemolytic anemia, thrombocytopenia, agranulocytosis
Nervous system: Sedation, sleepiness, dizziness, disturbed coordination, fatigue, confusion, restlessness, excitation, nervousness, tremor, irritability, insomnia, euphoria, paresthesia, blurred vision, diplopia, vertigo, tinnitus, acute labyrinthitis, neuritis, convulsions
Gastrointestinal: Epigastric distress, anorexia, nausea, vomiting, diarrhea, constipation
Genitourinary: Urinary frequency, difficult urination, urinary retention, early menses
Respiratory: Thickening of bronchial secretions, tightness of chest and wheezing, nasal stuffiness
Interference with laboratory tests: Diphenhydramine will interfere with wheal formation in skin testing for skin sensitizing reaginic antibodies. However, the drug does not interfere with serological tests for IgE such as radioallergosorbent test.

OVERDOSAGE AND MANAGEMENT

Diphenhydramine overdosage in adults causes CNS depression with drowsiness or coma which may be followed by excitement, seizures, and postictal depression. Impaired consciousness, psychosis, tachycardia and mydriasis have also been reported.
The following signs and symptoms of overdosage have been reported in children: psychosis, fixed dilated pupils, abnormal eye movements, flushed face, dry mouth, urinary retention, fever, excitation, hallucinations/delusions, disorientation, agitation, confusion, jitteriness, restlessness, irritability, hyperactivity, delirium, twitching, tiredness, abnormal tongue movement, unsteady pattern of walking, trembling extremities, slurred speech, ataxia, athetosis, seizures, and postictal depression.
Treatment should be supportive and directed towards specific symptoms.
If vomiting has not occurred spontaneously the patient should be induced to vomit. This is best done by having him drink a glass of water or milk after which he should be made to gag. Precautions against aspiration must be taken, especially in infants and children.
If vomiting is unsuccessful, gastric lavage is indicated within three hours after ingestion and even later if large amounts of milk or cream were given beforehand. Isotonic or (1/2) isotonic saline is the lavage solution of choice.
Saline cathartics, such as milk of magnesia, draw water into the bowel by osmosis and therefore are valuable for their action in rapid dilution of bowel content.
Stimulants should not be used.
Vasopressors may be used to treat hypotension. Convulsions and marked CNS stimulation should be treated with parenteral diazepam.

CAUTION: Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

ADVERSE DRUG REACTION REPORTING STATEMENT

For suspected adverse drug reaction, seek medical attention immediately and report to the FDA at www.fda.gov.ph **AND** Unilab at (+632) 858-1000 or productsafety@unilab.com.ph.
By reporting undesirable effects, you can help provide more information on the safety of this medicine.

AVAILABILITY :

* Soniphen 50mg Capsule- Alu flex foil strips X 10's (Box of 30's)-DR-XY38500
** Soniphen 50mg Solution for Injection - Amber Glass Ampule X 1 mL (Box of 10's)-DR-XY37655

* Store at temperatures not exceeding 30°C. Keep the product out of sight and reach of children.
** Store at temperatures not exceeding 30°C. Keep the product out of sight and reach of children. Protect from direct sunlight.

Date of First Authorization:
* January 9, 2012
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Trusted Quality Healthcare

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